1: Tumori 1987 Feb 28;73(1):1-9

Related Articles, Link

Growth inhibition of murine colonic adenocarcinoma by tumor immune but not by IL-2-activated or alloactivated lymphocytes.

Rodolfo M, Parmiani G.

The antigenic profile of C-26 and C-51 BALB/c colonic adenocarcinomas was examined by in vivo and in vitro assays. Mice immunized with irradiate C-26 or C-51 tumor cells from freshly excised tumor nodules or from in vitro-growing cell lines were able to reject a challenge of both tumors. Spleen lymphocytes of immune but not of normal mice were effective in cross-inhibiting tumor growth in vivo in a Winn assay. Tissue-associated antigens common to C-26 and C-51 and to their metastases but not to other syngeneic neoplasms were detected in vitro by cytotoxic T lymphocytes obtained after 5 days of a secondary culture of immune lymphocytes and irradiated tumor cells. Activated lymphocytes were obtained by exposure of spleen cells to interleukin 2 or by allostimulation. Such lymphocytes, although cytotoxic in vitro on C-26 and C-51 carcinomas, were unable to significantly reduce in vivo tumor growth in the Winn assay.

PMID: 3493573 [PubMed - indexed for MEDLINE]

Display Abstract Show: 20 Sort Send to Text

WEST

Generate Collection | Print

L1: Entry 1 of 2 File: USPT Mar 27, 2001

US-PAT-NO: 6207147
DOCUMENT-IDENTIFIER: US 6207147 B1

TITLE: Cancer immunotherapy using tumor cells combined with mixed lymphocytes

DATE-ISSUED: March 27, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hiserodt; John C.	Huntington Beach	CA		
Thompson; James A.	Aliso Viejo	CA		
Granger; Gale A.	Laguna Beach	CA		

US-CL-CURRENT: 424/93.1; 424/93.3, 435/347, 435/363, 435/366, 435/372, 435/373, 435/374

CLAIMS:

What is claimed as the invention is:

1. An immunogenic composition suitable for administration to a human, comprising an effective combination of:

a) stimulated lymphocytes allogeneic to the human; and

b) tumor-associated antigen from the human;

wherein the combination is effective to elicit an immune response to the tumor-associated antigen in the human subject after administration.

2. The immunogenic composition of claim 1, wherein said tumor-associated antigen is comprised in a primary tumor cell from said human, or a progeny of such a tumor cell obtained by culturing the tumor cell ex vivo.

3. The immunogenic composition of claim 1, wherein said tumor-associated antigen is comprised in an extract of a primary tumor cell from said human, a progeny of a primary tumor cell from said human, or a combination thereof.

4. The immunogenic composition of claim 1, wherein said stimulated lymphocytes have been stimulated by culturing with leukocytes allogeneic to the lymphocytes.

5. The immunogenic composition of claim 1, where said stimulated lymphocytes have been stimulated by culturing with a recombinantly produced cytokine, a mitogen, or with a cell genetically altered to secrete a cytokine at an elevated level.

6. An immunogenic composition suitable for administration to a humans, comprising an effective combination of:

a) lymphocytes allogeneic to the human;

b) leukocytes allogeneic to the lymphocytes; and

c) an inactivated tumor cell population, consisting essentially of primary tumor

cells obtained from the human, or the progeny of such cells;

wherein the combination is effective to elicit an immune response to the tumor cell population in the human subject after administration.

7. The immunogenic composition of claim 6, wherein the leukocytes are autologous to the human.

8. The immunogenic composition of claim 6, wherein the leukocytes are allogeneic to the human.

9. The immunogenic composition of claim 6, comprising leukocytes from at least three different human donors.

10. The immunogenic composition of claim 6, wherein the inactivated tumor cell population are selected from the group consisting of melanoma, pancreatic cancer, liver cancer, colon cancer, prostate cancer, and breast cancer cells.

11. The immunogenic composition of claim 6, wherein the leukocytes are inactivated.

12. The immunogenic composition of claim 6, wherein said lymphocytes comprise a cell that has been genetically altered to express a cytokine at an elevated level.

13. The immunogenic composition of claim 6, wherein said leukocytes and said lymphocytes are cocultured for a duration and under conditions sufficient for allogeneic stimulation of the lymphocytes, prior to combination with said tumor cell population.

14. The immunogenic composition of claim 6, wherein said coculturing is for a duration and under conditions sufficient to stimulate elevated cytokine secretion by the lymphocytes.

15. A unit dose of the immunogenic composition according to claim 6, wherein the number of said lymphocytes allogeneic to the leukocytes in the dose is between about 1.times.10.sup.8 and 2.times.10.sup.9.

16. A unit dose of the immunogenic composition according to claim 6, wherein the inactivated tumor cell population in the dose consists of between about 1.times.10.sup.6 and 5.times.10.sup.7 cells.

17. A method for producing the immunogenic composition of claim 1, comprising mixing:

a) stimulated lymphocytes allogeneic to said human; with

b) tumor-associated antigen from the human.

18. A method for producing the immunogenic composition of claim 1, comprising mixing:

a) cells obtained from a coculture of lymphocytes allogeneic to said human and leukocytes allogeneic to the lymphocytes; with

b) primary tumor cells from the human, or progeny thereof.

19. A kit for producing the immunogenic composition of claim 1, comprising in separate containers:

a) stimulated lymphocytes allogeneic to the human; and

b) tumor-associated antigen from the human.

20. A kit for producing the immunogenic composition of claim 1, comprising in separate containers:

a) cells obtained from a coculture of lymphocytes allogeneic to said human and leukocytes allogeneic to the lymphocytes; and

b) primary tumor cells from the human, or progeny thereof.

21. A method for inducing an anti-tumor immunological response in a human, comprising administering an immunogenic amount of the immunogenic composition of claim 1 to the human.

22. A method for inducing an anti-tumor immunological response in a human, comprising administering an immunogenic amount of the immunogenic composition of claim 6 to the human.

23. A method for stimulating an anti-tumor immunological response in a human, comprising the steps of:

a) mixing ex vivo a first cell population comprising tumor cells, and a second cell population comprising lymphocytes allogeneic to the human, to produce a cell mixture; and

b) administering an immunogenic amount of the cell mixture to the human.

24. The method of claim 23, wherein said tumor cells comprises cells selected from the group consisting of melanoma, pancreatic cancer, liver cancer, colon cancer, prostate cancer, and breast cancer.

25. The method of claim 23, wherein said second cell population further comprises leukocytes allogeneic to the lymphocytes.

26. The method according to claim 23, wherein the second cell population contains leukocytes from at least three different human donors.

27. The method of claim 23, wherein the leukocytes are autologous to the human.

28. The method of claim 23, wherein the leukocytes are allogeneic to the human.

29. The method of claim 23, wherein said immunological response is a primary response.

30. The method of claim 23, wherein said immunological response is a secondary response.

31. The method of claim 23, wherein said human has been previously treated by administration of alloactivated allogeneic lymphocytes into a solid tumor in the human or at or around a site where a solid tumor or a portion thereof has been removed.

32. A method for treating a neoplastic disease in a human, comprising administering an effective amount of the immunogenic composition of claim 6 to the human.

33. A method for treating a neoplastic disease in a human, comprising the steps of:

a) mixing ex vivo a first cell population comprising tumor cells, and a second cell population comprising lymphocytes allogeneic to the human, to produce a cell mixture; and

b) administering an effective amount of the cell mixture to the human.

34. The method of claim 33, wherein said second cell population further comprises leukocytes allogeneic to the lymphocytes.